12. (new) An artificial antigen presenting cell according to claim 1 wherein the neutral phospholipids are phosphotidylcholine.

13. (new) An artificial antigen presenting cell according to claim 6 wherein the neutral phospholipids are phosphotidylcholine.

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14. (new) An artificial antigen presenting cell according to claim 1 wherein the lipid bilayer is a fluid lipid bilayer.

15. (new) An artificial antigen presenting cell according to claim 1 wherein the lipid bilayer is a fluid lipid bilayer.

Remarks

A. Interview.

As an initial matter, Applicant thanks the Examiner for meeting with the his undersigned attorney on 25 March 2003 to discuss this application (the "Interview").

B. Status of Claims.

Claims 1–11 are pending. Herein, claims 1, 2, 6, and 7 have been amended, claims 4, 5, 9, and 11 have been canceled, and new claims 12-15 have been added. Thus, after entry of this amendment, claims 1-3, 6-8, 10, and 12-15 will be pending. Accordingly, Applicant's remarks below are directed to these claims. Please also note that each of the above amendments is fully supported by the specification and adds no new matter.

The amendments to claims 1, 2, 6, and 7 simply reflect Applicant's desire to use preferred terminology and focus examination on certain preferred, commercially significant embodiments of the invention, as discussed during the Interview. For example, in each of independent claims 1 and 6, part (a) has been amended to reflect preferred embodiments wherein the lipid bilayer of the artificial antigen presenting cells ("aAPCs") of the invention contains neutral phospholipids and cholesterol. The specification is replete with support for

this amendment. See, e.g., specification page 21, lines 9-11. Claims 1 and 6, and dependent claims 2 and 7, have also been amended by adding the term "ganglioside" after "GM-1", support for which is found at specification page 13, lines 18-21. Also, the term "associated with" has been replaced with "bound to" in these claims, as suggested in Paper 10. It should be understood, however, that this amendment is not to be interpreted to require covalent linkage, but instead encompasses any specific interaction, be it covalent or non-covalent, between the respective members referred to as being bound to each other.

New claims 12 and 13 are directed to embodiments of the invention wherein the neutral phospholipids are phosphotidylcholine molecules. Support for these claims is found at various locations in the specification. For example, see page 25, line 22.

Newly added claims 14 and 15 concern aAPCs wherein the lipid bilayer is "fluid", i.e., its nature is such that the constituents thereof (e.g., lipids, proteins, etc.) are "free-floating," meaning that they can diffuse laterally in the membrane. The "free-floating" nature of the lipid bilayer is mentioned at numerous places in the specification. See, e.g., specification page 12, lines 12-15, and page 13, lines 26-28. As explained at page 12 of the specification, this feature allows the aAPCs of the invention to, for example, promote T cell "capping", which is important in T cell activation, by allowing elements necessary for this activity to accumulate at the T cell/aAPC interface. See, e.g., Figures 1 and 16-18, and the corresponding descriptions thereof at specification page 35, line 27, through page 36, line 10, and page 38, line 19, through page 39, line 12, respectively. Because of this feature, molecules disposed in the membrane, e.g., GM-1 ganglioside molecules, can also associate to form "rafts". Applicant respectfully submits that the concept of "free floating" membrane components is synonymous with the concept of "membrane fluidity," which is enshrined in modern biology as the "fluid mosaic model" of membrane structure, whose name indicates the movement of both lipids and proteins in membranes.

Claims 4, 5, 9, and 11 have been cancelled without prejudice to advance prosecution in light of the finality of the earlier-advanced restriction requirement concerning these claims.

Applicant respectfully requests reconsideration of the invention in view of the above amendments. It is understood, however, that Applicant reserves the right to pursue subject

matter no longer or not yet claimed in this application in this or another application that claims priority hereto.

C. Argument.

1. Color Photographs.

Applicant respectfully requests that the objection raised in Paper 10 with regard to color photographs be held in abeyance until such time as it is determined that the claims are in condition for allowance. At that time, Applicant will amend the specification as necessary and file the requisite petition, fee, and three sets of photographs.

2. 35 U.S.C. § 112, Second Paragraph.

Paper 10 contains three rejections alleging that the invention as previously claimed failed to comply with the definiteness requirement of 35 U.S.C. § 112, second paragraph. Applicant respectfully disagrees with this assessment. Applicant respectfully submits that, prior to the amendment above, those ordinarily skilled in the art would have understood the metes and bounds of the invention in view of the terminology used. That said, to advance prosecution, Applicant has elected to amend the pending claims to obviate these issues. Accordingly, these rejections can be withdrawn.

3. 35 U.S.C. § 112, First Paragraph – Written Description.

Paper 10 asserts that the claims under examination lack an adequate written description, as required by 35 U.S.C. § 112, first paragraph, due to the terms "associated with" and "at least a portion of". Applicant again respectfully disagrees, for two reasons. First, those ordinarily skilled in the art would understand these terms as used in the claims. Second, the purpose of the "written description" requirement of 35 U.S.C. § 112, first paragraph, is a notice provision to show that a patent applicant actually possessed the claimed invention at the time of filing, and the use of these terms does not negatively influence that showing. To advance prosecution, however, Applicant has again elected to amend the

pending claims to remove the allegedly objectionable terminology, thereby obviating the bases of this rejection. As such, Applicant respectfully requests that it be withdrawn.

4. 35 U.S.C. § 112, First Paragraph – Enablement.

Lastly, it is contended in Paper 10 that the specification fails to satisfy the "enablement" requirement of 35 U.S.C. § 112, first paragraph, with regard to the pending claims. Applicant respectfully traverses, both with regard to the claims pending prior to and after entry of the amendment above, because in either case the specification teaches those of ordinary skill in the art how to make and use the invention without undue experimentation.

To begin with, Applicant's invention is pioneering in nature, because using the claimed aAPCs, it is possible efficiently isolate and manipulate antigen-specific T cells. Moreover, Applicant's invention concerns only liposomes comprised of lipid bilayers which minimally contain the novel, non-obvious combination of one or more GM-1 ganglioside molecules disposed therein and to which a cholera toxin beta subunits are bound or associated, antigen-loaded MHC components bound to or associated with the cholera toxin beta subunits, and accessory molecules that stabilize T cell receptor/antigen-loaded MHC component interactions. Moreover, as amended above, the claims now concern preferred embodiments wherein the lipid bilayer that forms the liposome is comprised of neutral phospholipids and cholesterol. Such liposomes are fluid under physiological conditions, and components disposed therein can readily diffuse laterally through the lipid bilayer. In this way, components can become concentrated in one or more areas on the liposome, as opposed to being randomly distributed. Indeed, the specification is replete with descriptions of the "free-floating" nature of the lipid bilayer of the aAPCs of the invention. Lipid bilayers comprised of neutral phospholipids and cholesterol represent preferred examples of how to provide this feature. In light of these teachings, and the known state of the art related to liposomes in general, Applicant respectfully submits that those of ordinary skill could by routine experimentation develop lipid bilayers having the this feature. Finally, nothing in the art teaches or suggests the inclusion of the other elements required by the claims, either before or after amendment.

For these reasons, Applicant contends that it is clear that the specification enables the full scope of Applicant's invention as now (and even previously) claimed, and he thus respectfully requests that the instant 35 U.S.C. § 112, first paragraph, rejection, be withdrawn.

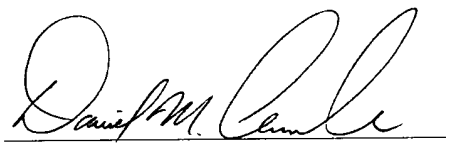
Conclusion

Herein, Applicant has amended certain of the pending claims, canceled others, added four new dependent claims, and demonstrated the patentability of the invention now claimed. As such, Applicant respectfully solicits a notice of allowable subject matter.

Due to the importance of this application to the assignee, Androclus Therapeutics, SpA, Applicant respectfully requests that if any issue remains that can be dealt with appropriately without the need for a formal action and response thereto, the Examiner telephone the undersigned at his earliest convenience so that the same may be expeditiously resolved.

Respectfully submitted,

Dated: 30 MAY 2003

By: 

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Appendix A

Version with marking to show changes made.

Below please find a copy of the amended claims to show all changes in the version of the claims now pending. Below, added material is underlined and deleted material is interlinated.

1. (twice amended) An artificial antigen presenting cell, comprising:
   f) a liposome comprising a lipid bilayer, wherein the lipid bilayer is comprised of neutral phospholipids and cholesterol;
   g) at least one GM-1 ganglioside molecule disposed in the lipid bilayer;
   h) [at least a portion] of a cholera toxin ß subunit bound to [associated with] a GM-1 ganglioside molecule;
   i) an [immunologically active] MHC component loaded with an antigen, wherein the antigen-loaded MHC component is bound to [associated with] the cholera toxin ß subunit; and
   j) an accessory molecule that can stabilize an interaction between a T cell receptor and the antigen-loaded MHC component.

2. (twice amended) An artificial antigen presenting cell according to claim 1 having a plurality of GM-1 ganglioside molecules, wherein a portion of the GM-1 ganglioside molecules form rafts in the lipid bilayer of the liposome.

6. (twice amended) An artificial antigen presenting cell, comprising:
   g) a liposome comprising a lipid bilayer, wherein the lipid bilayer is comprised of neutral phospholipids and cholesterol;
   h) at least one GM-1 ganglioside molecule disposed in the lipid bilayer;
   i) [at least a portion of] a cholera toxin ß subunit bound to [associated with] a GM-1 ganglioside molecule;
   j) at least one tetravidin molecule bound to [associated with] the cholera toxin ß subunit [lipid bilayer];

k) [an immunologically active] a biotinlylated MHC component loaded with an antigen, wherein the biotinlylated MHC component loaded with antigen is [associated with] bound to the tetravidin molecule of (d) [cholera toxin ß subunit]; and

l) [an] a biotinlylated accessory molecule that can stabilize an interaction between a T cell receptor and the antigen-loaded MHC component, wherein the biotinlylated accessory molecule is bound to [associated with a] the tetravidin molecule of (d).

7. (twice amended) An artificial antigen presenting cell according to claim 6 having a plurality of GM-1 ganglioside molecules, wherein a portion of the GM-1 ganglioside molecules form rafts in the lipid bilayer of the liposome.

12. (new) An artificial antigen presenting cell according to claim 1 wherein the neutral phospholipids are phosphotidylcholine.

13. (new) An artificial antigen presenting cell according to claim 6 wherein the neutral phospholipids are phosphotidylcholine.

14. (new) An artificial antigen presenting cell according to claim 1 wherein the lipid bilayer is a fluid lipid bilayer.

15. (new) An artificial antigen presenting cell according to claim 1 wherein the lipid bilayer is a fluid lipid bilayer.